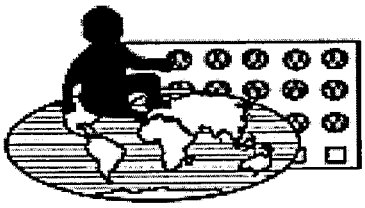

Newborn Screening Quality Assurance Program

PROFICIENCY TESTING — Cystic Fibrosis Quarterly Report

Volume 4, No. 1 February 2005

INTRODUCTION

The Cystic Fibrosis (CF) proficiency testing (PT) report is the quarterly summary of all data reported within the specified data-reporting period for Quarter 1, 2005. The attached tables provide the certification profiles (Immunoreactive Trypsinogen and DNA) for the distributed specimens, the verification of your reported data, the statistical analysis of the quantitative data, and the frequency distributions summary for presumptive clinical (qualitative) assessments. We distribute this PT report to all participants, state laboratory directors, and program colleagues by request.

On January 10, 2005, a panel of five unknown dried-blood-spot (DBS) specimens enriched with predetermined concentrations of IRT was distributed to 11 laboratories in the United States and 46 laboratories in other countries.

PARTICIPANTS' RESULTS

We processed data from 45 participants. Laboratories were asked to report IRT results in ng/mL blood. For the statistical summary analysis, we did not include data that were outside the 99% confidence interval. There were eleven outliers for this survey. Results of our evaluation suggest that the endogenous level of IRT was less than 15 ng/mL blood.

Sixteen laboratories reported using Delfia to measure IRT, 19 used AutoDelfia, 2 used MP Biomedicals (ICN), 2 used Bioclone, 3 used BioRad Quantase, and the remaining 3 reported using "other." The expected IRT values are based on CDC assayed values. IRT is stable in the dried blood matrix. Table 1 illustrates comparability of the recovery of IRT from each specimen by method.

Presumptive clinical classifications (qualitative assessments) may differ by participant because of specific assessment practices. For participants that have provided us with their IRT cutoff value, we applied that cutoff in our final appraisal of the error judgment. Overall, participants reported no false-positive clinical assessments and two false-negative clinical assessments. Domestic and foreign laboratories reported various cutoffs for IRT. The median and mode cutoffs for domestic participants were 96.5 ng/mL blood and 90 ng/mL blood, respectively. The median and mode cutoffs for foreign participants were 67.0 ng/mL blood and 70 ng/mL blood, respectively.

We distributed DBS specimens containing DNA from Epstein-Barr virus-transformed lymphoblastoid cell lines homozygous for ΔF508 in a sheep whole blood matrix (specimens 1584 and 1585). These specimens were enriched with IRT to create proficiency testing materials that expressed both phenotype (elevated IRT) and genotype (ΔF508) for CF.

Participants were asked to confirm specimens that screened IRT positive. Fifteen laboratories reported DNA confirmatory results. Six laboratories reported using PCR amplification of DNA, 2 used Roche Linear Array, 2 used Orchid Bioscience Elucigene, 2 used Innogenetics Auto-Lipa method, 1 used Fluorescence Polarization, and 2 used Oligonucleotide Ligation Assays. Two laboratories reported an incorrect CF confirmed clinical assessment of ΔF508/Wild Type for specimen 1584 and one laboratory reported an incorrect CF confirmed clinical assessment of ΔF508/Wild Type for specimen 1585. One laboratory did not test specimen 1585 for DNA although it was correctly identified as having elevated IRT. Two laboratories could not report data because of problems with amplifying specimens. We are continuing to evaluate our methods for preparing these specimens to avoid amplification failures by participants.❖

The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis PT specimens on April 4, 2005.❖

CDC/APHL

This program is cosponsored by the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL).

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NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS - IRT

QUARTER I - FEBRUARY 2005

LAB XXX

SPECIMEN CERTIFICATION - IRT

CDC ASSAYED LEVELS

Analyte	Specimen 1581	Specimen 1582	Specimen 1583	Specimen 1584	Specimen 1585
Immunoreactive Trypsinogen CDC Mean Assayed Value (ng/mL blood)	12.6 ± 3.7	20.1 ± 3.1	15.9 ± 2.9	149.5 ± 16.4	180.2 ± 14.1

EXPECTED PRESUMPTIVE CLINICAL ASSESSMENTS

Disorder	Specimen 1581	Specimen 1582	Specimen 1583	Specimen 1584	Specimen 1585
Cystic Fibrosis	01	01	01	02	02

01 = within normal limits 02 = outside normal limits NE = clinical assessment not evaluated

DATA VERIFICATION

Analyte	Specimen 1581		Specimen 1582		Specimen 1583		Specimen 1584		Specimen 1585	
	Result	Code	Result	Code	Result	Code	Result	Code	Result	Code
Immunoreactive Trypsinogen (ng/mL blood)										

01 = within normal limits 02 = outside normal limits NE = clinical assessment not evaluated

Reviewer's Comments

EVALUATION:

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS - IRT

QUARTER I - FEBRUARY 2005

OVERALL STATISTICS - IRT

Specimen	N*	Outliers	Mean	UL (95%)	LL (95%)
1581	43	2	9.4	15.5	3.4
1582	42	3	18.4	26.2	10.6
1583	43	2	12.8	18.4	7.3
1584	43	2	133.5	188.4	78.5
1585	43	2	159	210.9	107.2

* Outliers are not included in N. UL = upper limit LL = lower limit

FREQUENCY DISTRIBUTION OF PARTICIPANTS' CLINICAL ASSESSMENTS

Specimen	Within Normal Limits	Outside Normal Limits
1581	44	0
1582	44	0
1583	44	0
1584	3	41
1585	0	44

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS - DNA

QUARTER I - FEBRUARY 2005

LAB XXX

SPECIMEN CERTIFICATION - DNA

CDC IDENTIFIED GENOTYPES

Analyte	Specimen 1581	Specimen 1582	Specimen 1583	Specimen 1584	Specimen 1585
DNA	Wild Type (Normal)	Wild Type (Normal)	Wild Type (Normal)	ΔF508/ΔF508	ΔF508/ΔF508

EXPECTED DNA CONFIRMED CLINICAL ASSESSMENTS

Disorder	Specimen 1581	Specimen 1582	Specimen 1583	Specimen 1584	Specimen 1585
Cystic Fibrosis	1, 4	1, 4	1, 4	2	2

1 = wild type (normal) 2 = cystic fibrosis positive 3 = cystic fibrosis carrier 4 = not tested

DATA VERIFICATION

Analyte	Specimen 1581		Specimen 1582		Specimen 1583		Specimen 1584		Specimen 1585	
	Result	Code	Result	Code	Result	Code	Result	Code	Result	Code
DNA										

1 = wild type (normal) 2 = cystic fibrosis positive 3 = cystic fibrosis carrier 4 = not tested

Reviewer's Comments

EVALUATION:

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS - DNA

QUARTER I - FEBRUARY 2005

SUMMARY OF PARTICIPANTS' GENOTYPES

Specimen	Genotype	N
1581	Wild Type/Wild Type	2
1582	Wild Type/Wild Type	2
1583	Wild Type/Wild Type	2
1584	ΔF508/ΔF508 ΔF508/Wild Type	10 2
1585	ΔF508/ΔF508 ΔF508/Wild Type	11 1

FREQUENCY DISTRIBUTION OF PARTICIPANTS' CLINICAL ASSESSMENTS

Specimen	Wild Type (Normal)	Cystic Fibrosis Positive	Cystic Fibrosis Carrier	Not Tested
1581	2	0	0	13
1582	2	0	0	13
1583	2	0	0	13
1584	0	10	2	1
1585	0	11	1	1

NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS - IRT

QUARTER I - FEBRUARY 2005

IMMUNOREACTIVE TRYPSINOGEN BY METHOD

Table 1. Recovery of IRT (ng/mL blood) by method

Specimen No.	Specimen 1581	Specimen 1582	Specimen 1583	Specimen 1584	Specimen 1585
Expected Value	12.6	20.1	15.9	145.9	180.2
Method (N)					
Delfia (16)	8.3 ± 4.3	16.1 ± 4.5	11.8 ± 3.8	141.2 ± 23.0	163.2 ± 17.8
AutoDelfia (19)	10.3 ± 1.4	19.8 ± 3.2	13.0 ± 2.1	140.7 ± 17.4	165.4 ± 20.9
MP (ICN) (2)	14.2 ± 3.5	23.8 ± 3.9	17.3 ± 1.7	149.9 ± 40.0	190.9 ± 17.7
Bio-Rad (3)	5.6 ± 1.7	14.0 ± 2.6	9.3 ± 3.0	70.1 ± 22.8	113.9 ± 20.4
Bioclone (2)	9.3 ± 1.0	15.4 ± 0.8	12.0 ± 0.1	52.2 ± 15.3	71.1 ± 0.1
Other (3)	11.7 ± 7.0	32.3 ± 8.0	18.4 ± 5.8	99.3 ± 28.5	115.8 ± 18.4

N = Number of observations